

## REMARKS

By an Office Action dated October 3, 2001 in the file of the above-identified patent application, the Examiner in charge of this application rejected all the pending claims of the application based on a variety of objections and based on the prior art. By this response, the applicant is responding to each and every one of those grounds of rejection. Reconsideration of the merits of this patent application is respectfully requested in view of this submission.

The first ground of rejection raised was under 35 U.S.C. §112, first paragraph. The Examiner conceded that the specification is enabling for a method of cultivating primate and human embryonic stem cells which, the Examiner conceded, were pluripotent. However, the Examiner objected to the claims because they failed to have the word "pluripotent" inserted in them. The applicant respectfully requests that this rejection be reconsidered.

The applicant does not contend that the stem cells claimed in this invention are not pluripotent. Primate embryonic stem cells described and used in the process of the present invention are clearly pluripotent. These primate embryonic stem cells may also be totipotent. However, as the Examiner is aware, certain of the tests necessary to establish that the cells are totipotent are not ethically permitted in the United States. Accordingly, while it is believed that the cells are probably totipotent, definitive scientific evidence of that has not been developed, at least to the knowledge of the applicant here.

Nevertheless, the applicant asserts that it would be unfair to the applicant, and contrary to the regularly established understanding of the term, for the applicant to be forced to add a word to his claim which could later be argued to be limiting. Note that the scientific community, and the federal government, have adopted and recognized consistent terminology to refer to the cells of the type described and claimed in the method claims of the present invention. That terminology is "primate (or human) embryonic stem cells." See, for example, the website at <http://escr.nih.gov> in which the federal government has announced its "stem cell registry." The title of the registry is "NIH Human Embryonic Stem Cell Registry." The very cells described in the examples of this patent application, stem cell line H9, are specifically listed on the registry (under the heading Wisconsin Alumni Research Foundation, providers code H9). Also from the stem cell registry web page, there is a link to another page providing NIH stem cell information. That page may be found at <http://www.nih.gov/news/stemcell/scireport.htm>. That report also uses the term "embryonic stem cells" to fully and completely describe the stem cells of the type described in the present

invention.

It is therefore asserted by the applicant here that the correct terminology to refer to the cells described in the present invention is "primate embryonic stem cells." The Examiner is attempting to force the applicant to insert a word, "pluripotent," the effect of which is to provide potential infringers a mechanism by which they can argue that their cells do not come within the claims of the present invention, i.e., by demonstrating that their stem cells are totipotent. Since the stem cells described herein are probably totipotent, and only at adherence to the ethical requirements prevalent in the United States has prevented a demonstration of that totipotency, it would be unfair and incorrect to require the applicant to insert a limiting term in his claims which is not needed by the art, and which is contrary to the recognized terminology utilized by the United States government in referring to cells of this type. Accordingly, it is respectfully requested that the Examiner reconsider and withdraw this ground of rejection.

Also under 35 U.S.C. §112, second paragraph, the Examiner objected to the words "essentially free of" on the grounds that that phraseology was indefinite. It is asserted by the applicant here that that phrase is completely definite and generally acceptable in patent claims. In Ex parte Kaiser, 69 U.S.P.Q. 185, the CCPA specifically held that the term "substantially free from" was definite within the ambit of 35 U.S.C. §112, second paragraph. It is submitted that "essentially free of" is an exact verbal equivalent to "substantially free from." If the Examiner disagrees, the applicant is willing to change its verbiage to a specifically tract the language which was previously approved by the CCPA. In any event, it is asserted by the applicant that the language is definite and recites that there is substantially no added fetal serum in the culture medium. The fact is that some of the constituents of the medium can be purified from serum, such as serum albumin, and therefore it may be possible to argue that minor contaminants of serum remain. It is for that reason that this term is used, and the term is believed to be used in a way that is both accurate and clearly understandable by those of ordinary skill in the art.

The Office Action next contains a rejection under §112, second paragraph, to Claims 15 and 16. Since those claims have been withdrawn, no remarks will be made herein about that issue.

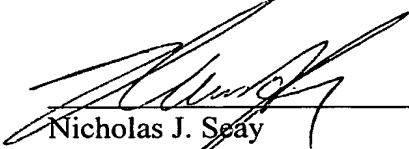
Beginning on page 8 of the Office Action and continuing on to page 12 of the Office Action are a series of rejections under §102 to Claims 15 and 16. Those claims have been

withdrawn by this response and hence no further remarks will be directed toward those particular claims.

Page 12 of the Office Action has a rejection under 35 U.S.C. §103 on the grounds that the invention claimed in this application is obvious over a combination of two patents to Hogan et al. and the scientific paper to Goldsborough et al. The Examiner notes that the derivation of human pluripotent cells is old in the art. However, that is not what is claimed in this patent application. The Examiner also correctly notes that Goldsborough et al. teaches a serum free culturing medium for murine embryonic stem cells. The Examiner contends from that that it would be obvious to substitute a medium such as used by Goldsborough which is serum free in the cultivation of human pluripotent cells of the type described by Hogan. The applicant believes that it might be obvious to try a serum free medium such as Goldsborough to create human pluripotent cells, but it is not at all obvious that it would actually work to successfully culture human embryonic stem cells in culture.

Techniques, media and conditions for the cultivation of stem cells of a variety of origins have varied from animal species to animal species. It is possible to create stem cell cultures from some species and not from others, even using similar techniques. Accordingly, it would not be predictable from the reference to Goldsborough that a serum free medium could be defined that would work with human embryonic stem cells. The Examiner's rejection is a classic "obvious to try" rejection. Neither patent to Hogan et al., nor the Goldsborough et al. paper, provide a reasonable expectation of success in using a serum free media to cultivate human embryonic stem cells. Accordingly, the method as described in this invention cannot be made obvious by the cited prior art. Accordingly it is requested that this ground of rejection be reconsidered and withdrawn.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Applicant: James A. Thomson

Date: April 3, 2002

Serial No.: 09/522,030

Group Art Unit: 1632

Filed: 03/09/2000

Examiner: J. Woitach

For: SERUM FREE CULTIVATION OF PRIMATE  
EMBRYONIC STEM CELLS

File No.: 960296.96544

1. (Amended) A method of culturing primate embryonic stem cells, comprising:  
culturing the primate embryonic stem cells in a culture essentially free of mammalian  
fetal serum and in the presence of fibroblast growth factor that is supplied from a source other  
than just a fibroblast feeder layer.

14. (Amended) A culture system for culturing primate embryonic stem cells,  
comprising:

a fibroblast feeder layer; and  
fibroblast growth factor supplied by other than just the fibroblast layer;  
wherein the culture system is [essentially] free of added animal serum.

17. (New) A method of culturing primate embryonic stem cells, comprising:  
culturing the primate embryonic stem cells in a culture free of added mammalian fetal  
serum and in the presence of fibroblast growth factor that is supplied from a source other than  
just a fibroblast feeder layer.

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